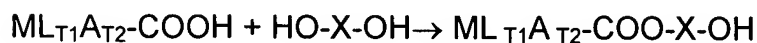




I. AMENDMENTS TO THE CLAIMS:

1. (Currently Amended) A process for the manufacture of NO-donating compounds comprising;

(1),



(I)

(II)

using an acidic or dehydrating agent and a first solvent, optionally followed by purification using extraction or crystallization, and

(2),

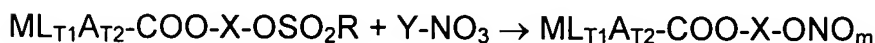


(II)

(III)

using a second solvent, a base and optionally a catalyst, followed by purification, and

(3),



(III)

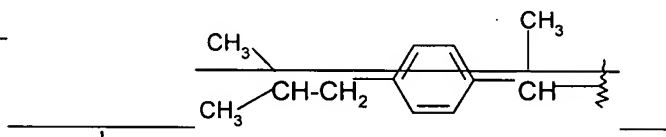
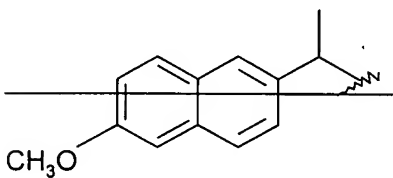
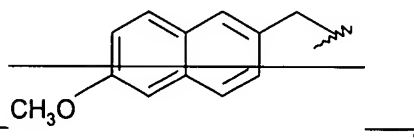
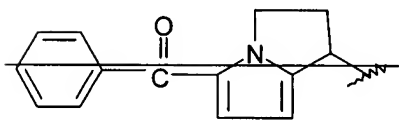
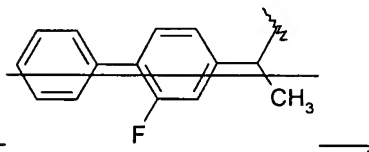
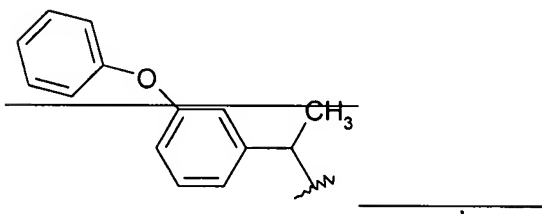
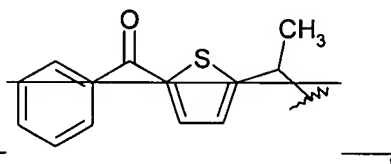
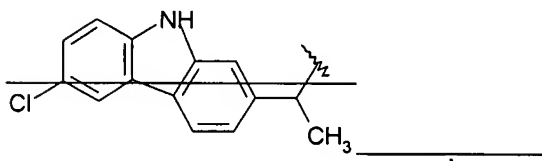
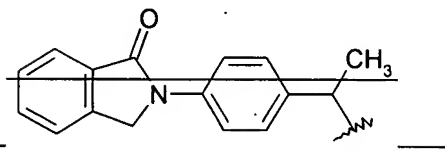
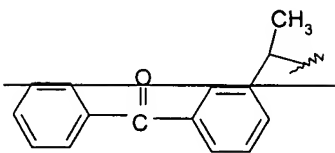
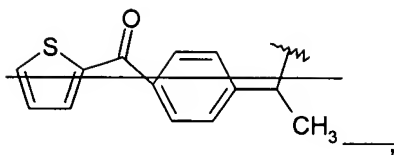
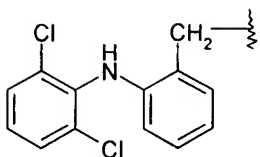
(IV)

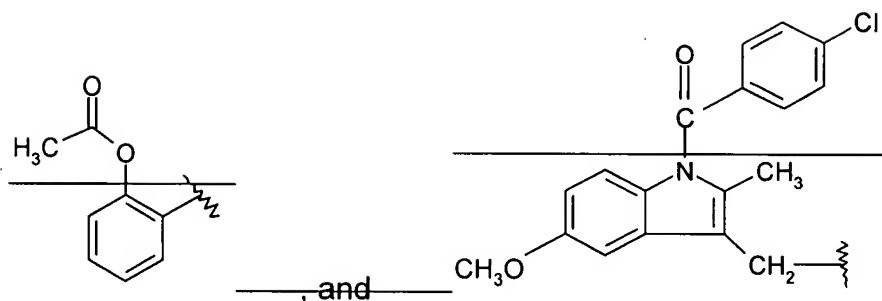
using a third solvent, at a maximum reaction temperature of 90°C, and optionally a catalyst,

optionally followed by a crystallization process for obtaining the compound of formula IV in a substantially crystalline form, and

wherein:

~~ML_{T1}A_{T2} is selected from the group consisting of :~~





X is selected from the group consisting of: linear $-(CH_2)_{w1}-$, wherein $w1$ is an integer of from 2 to 10; or $-(CH_2)_{w2}-O-(CH_2)_{w3}-$, wherein $w2$ and $w3$ are integers of from 2 to 10; ~~or~~ $(CH_2-CH_2-O)_2-CH_2-CH_2-$;

R is selected from the group consisting of C_1-C_8 alkyl;

$Y-NO_3$ is selected from the group consisting of lithium nitrate, sodium nitrate, potassium nitrate, magnesium nitrate, calcium nitrate, iron nitrate, zinc nitrate and tetraalkylammonium nitrate, wherein alkyl is a straight or branched C_1-C_{18} -alkyl, and a mixture thereof; and

m is 2; ~~and~~

~~with the proviso that when $ML_{T1}A_{T2}-COOH$ is naproxen, then X is not $(CH_2)_4$.~~

2-6. (Canceled)

7. (Previously Presented) The process according to claim 1, wherein the crystallization process for the compound of formula IV comprises:

a) i) dissolving the compound in a fourth solvent;

or,

- ii) extracting the compound from the reaction solution into a fourth solvent;
- or,
- iii) starting from the reaction solution comprising the compound;
- b) evaporating the fourth solvent;
- c) adding an anti-solvent and/or cooling
- d) isolating the crystals formed, and optionally;
- e) recrystallizing the crystals formed or isolated.

8. (Previously Presented) The process according to claim 7, wherein the crystallization process for compound 2-[2-(nitrooxy)-ethoxy]ethyl{2-[(2,6-dichlorophenyl)amino]phenyl}acetate (IVa) comprises:

- a) iii) starting from the reaction solution comprising the compound;
- b) evaporating the fourth solvent;
- c) adding isopropanol and cooling the resulting solution; and
- d) isolating the crystals formed.

9. (Currently Amended) The process according to claim 1, wherein the acidic or dehydrating agent is selected from the group consisting of sulphuric acid or its salts, perchloric acid, polystyrene sulphonic acids, zeolites, acidic clays, and in combination with strong hydrophilic acids, and montmorillonites.

10. (Previously Presented) The process according to claim 1, wherein the first solvent is a non-polar and/or non acidic solvent.

11. (Previously Presented) The process according to claim 1, wherein the second solvent is selected from a group consisting of toluene, cumene, xylenes, ethyl acetate, acetonitrile, butyl acetate, and isopropyl acetate.

12. (Previously Presented) The process according to claim 1, wherein the base is triethylamine or *N*-methylmorpholine.

13. (Previously Presented) The process according to claim 1, wherein the catalyst is 4-(dimethylamino)pyridine.

14. (Previously Presented) The process according claim 1, wherein the compound of formula III is crystallized from an organic solvent.

15. (Previously Presented) The process according to claim 14, wherein an anti-solvent is used in the crystallization of compound of formula III.

16. (Previously Presented) The process according to claim 1, wherein Y-NO₃ is selected from the group consisting of lithium nitrate, sodium nitrate, potassium nitrate, magnesium nitrate, calcium nitrate, and mixtures thereof.

17. (Previously Presented) The process according to claim 1, wherein the third solvent is selected from the group consisting of *N*-methylpyrrolidinone, sulpholane, tetramethylurea, 1,3-dimethyl-2-imidazolidinone, acetonitrile, methyl isobutylketone, ethyl acetate, butyl acetate, isopropyl acetate, and mixtures thereof.

18. (Previously Presented) The process according to claim 1, wherein the phase transfer-catalyst is selected from the group consisting of tetraalkylammonium salt, arylalkylammonium salt, tetraalkylphosphonium salt, arylalkylphosphonium salt, crown ether, pentaethylene glycol, hexaethylene glycol, polyethylene glycols, and mixtures thereof.

19. (Previously Presented) The process according to claim 7, wherein the fourth solvent is selected from the group consisting of lower alkyl acetates, lower alkyl alcohols, aliphatic hydrocarbons, aromatic hydrocarbons, heteroaromatic hydrocarbons, dialkyl ketones, dialkyl ethers, nitriles, water, and mixtures thereof.

20. (Previously Presented) The process according to claim 7, wherein the anti-solvent is selected from the group consisting of ethanol, 2-propanol, toluene, cumene, xylenes, ligroin, petroleum ether, halobenzenes, heptanes, hexanes, octanes, cyclohexanes, cycloheptanes, and mixtures thereof.

21. (Previously Presented) The process according to claim 7, wherein the solvent in step d) is selected from the group consisting of toluene, cumene, xylenes, methyl *iso*-butyl ketone, di-*n*-butyl ether, *tert*-butyl methyl ether, tetrahydrofuran, acetonitrile, *n*-butyl acetate, dichloromethane, and mixtures thereof.

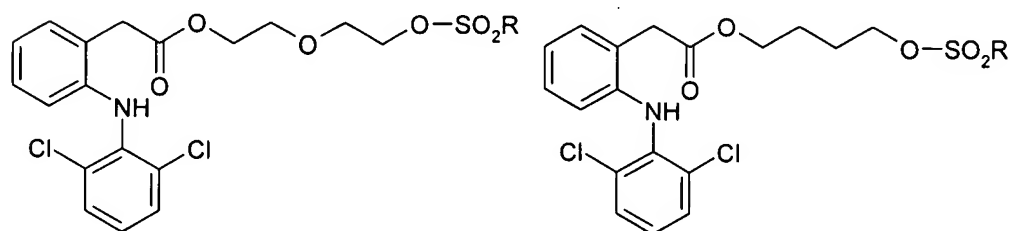
22. (Previously Presented) The process according to claim 1, wherein the process is conducted at a temperature below 130°C in (1) and (2).

23. (Canceled)

24. (Previously Presented) The process according to claim 1, wherein the chemical purity of Form A of compound IVa is above 95%.

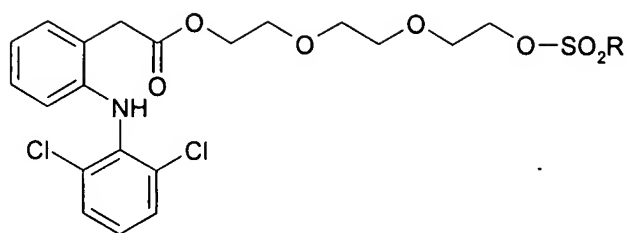
25-31. (Canceled)

32. (Withdrawn) Compounds of formula IIIa, IIIb, IIIc and IIId:

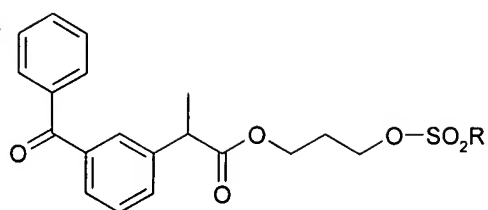


IIIa

IIIb



IIIc



IIId

wherein R is selected from the group consisting of C₁-C₈ alkyl.

33. (Canceled)

34. (Withdrawn) A method for manufacturing a pharmaceutically active compound comprising providing compounds of formula III, ML_{T1}A_{T2}-X-O-SO₂R, wherein M, L, A, T₁, T₂, X and R are as defined in claim 1, and manufacturing a pharmaceutically active compound from the compounds of formula III.

35. (Withdrawn) A method for preparing a medicament for the treatment of pain and/or inflammation comprising providing intermediate compounds of formula IIIa, IIIb, IIIc and

IIId as defined in claim 32, prepared according to the process described under step 1 and 2 of claim 1, manufacturing a pharmaceutically active compound from the compounds of formula IIIa, IIIb, IIIc and IIId, and combining the pharmaceutically active compound with one or more diluents, excipient or carriers.

36-38. (Canceled)

39. (Previously Presented) The process according to claim 1, wherein R is $-\text{CH}_3$.

40. (Currently Amended) A process according to claim 1, wherein Y-NO_3 of step (3) is sodium nitrate and tetrabutylammonium nitrate, the third solvent is a mixture of butyl acetate and acetonitrile, and step (3) is conducted at a temperature of 87°C .

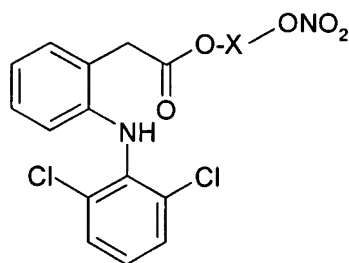
41. (Previously Presented) A process according to claim 1, wherein Y-NO_3 of (3) is sodium nitrate and tetrabutylammonium nitrate, the third solvent is a mixture of n-butyl acetate and water, and step (3) is conducted at a temperature of 90°C .

42. (Previously Presented) The process according to claim 1, wherein w_1 is 3 or 4, and w_2 and w_3 are 2.

43. (Previously Presented) The process according to claim 11, wherein the second solvent is selected from a group consisting of toluene, cumene, and xylenes.

44. (Previously Presented) The process according to claim 12, wherein RSO_2Cl is methanesulfonyl chloride and the base is *N*-methylmorpholine.

45. (Previously Presented) A process according to claim 1 for the manufacture of the compound of formula IVa

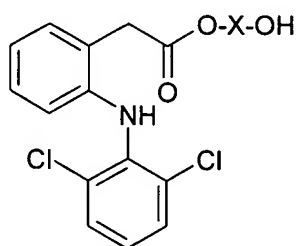


IVa

wherein $\text{X} = -\text{C}_2\text{H}_4\text{OC}_2\text{H}_4-$,

comprising:

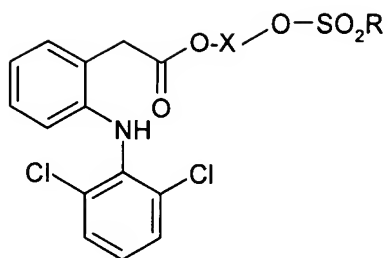
(1) reacting diclofenac with diethyleneglycol and concentrated sulphuric acid in toluene to obtain the compound of formula IIa



IIa

wherein $\text{X} = -\text{C}_2\text{H}_4\text{OC}_2\text{H}_4-$,

(2) reacting a solution of the compound of formula IIa in toluene, *N*-methyl morpholine and methanesulfonyl chloride to obtain the compound of formula IIIa

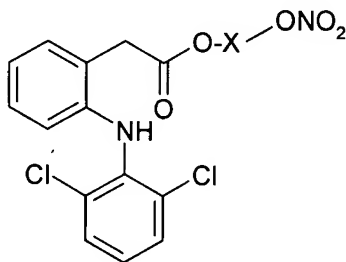


IIIa

wherein X = $-\text{C}_2\text{H}_4\text{OC}_2\text{H}_4-$ and R is $-\text{CH}_3$,

(3) purifying compound IIIa by crystallization; and

(4) reacting the crystallized compound of formula IIIa with lithium nitrate in N-methyl pyrrolidinone at a temperature of about 75°C to obtain the compound of formula IVa



IVa

wherein X = $-\text{C}_2\text{H}_4\text{OC}_2\text{H}_4-$.

46-49. (Canceled)